IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Skiffington et al.	Examiner:	Beisner, William H.
Reissue Serial No:	10/014,154	Art Unit:	1744
Filed:	December 6, 2001		
Original Patent:	6,180,395		
Original Patent Issue Date:	January 30, 2001		
Title:	Reagent Chamber For Test Apparatus and Test Apparatus		

SECOND DECLARATION OF DR. STEVEN J. SAUL

I declare:

1. I have been employed in the area of scientific research and development by Charm Sciences, Inc., the assignee of the above-captioned patent application, since 1990. I currently hold the position of Director of Research.

2. I have worked and published extensively in the area of protein chemistry and enzymatic reactions, and I am an expert in this field. In 1983, I was awarded a PhD degree in Biological Science, with an emphasis in enzymology, from the University of Rhode Island, RI. From 1984-1990, I conducted postdoctoral studies in several areas of enzymatic biochemistry, which included the protein biochemistry and reaction mechanisms of several insect systems. Attached, as Exhibit 1 hereto is my curriculum vitae, which lists over 32 publications in this scientific area of which I am an author or a co-author. My curriculum vitae further include seven issued patents in this scientific area of which I am an inventor or co-inventor. Exhibit 1.

3. I have extensive experience using and refining techniques for detecting ATP by the luciferin-luciferase enzymatic reaction, and with the use of lysis solutions to extract

ATP from cellular samples. I hold three U.S. patents which concern subject matter relating to the use of the luciferase enzyme with various derivatives of luciferin. See, Exhibit 1, page 3.

4. I have read the patent application US Serial No. 10/014,154, and have also read the Office Action issued on March 28, 2005.

5. I have reviewed the disclosure of US Patent 4,770,853, which issued on September 13, 1988, to David Bernstein of Sykesville, Maryland.

6. I have reviewed the disclosure EP 0309184, Simpson et al, 1991, "Method for ATP Extraction" (hereafter "Simpson").

7. I have reviewed the disclosure of US Patent 3,666,631, which issued on May 30, 1972, to Rich et al (hereafter "Rich").

8. I have reviewed the disclosure of Matsumoto et al., JP 7-59555 (hereafter "Matsumoto").

9. It is my opinion that one of ordinary skill in the art in 1995, reading the Bernstein, Simpson, and Rich patents, would not have been motivated to provide a unit dose reagent chamber containing a luciferin-luciferase reagent by placing luciferin-luciferase in the vessel of the Bernstein apparatus, because the Bernstein apparatus is not suitable for chemiluminescent detection of ATP, and because modification of the Bernstein apparatus for chemiluminescent detection of ATP would have made the Bernstein apparatus unsuitable for its intended purpose of a solid phase immunodiffusion assay.

10. It is my opinion that one of ordinary skill in the art in 1995, reading the Bernstein, Simpson, and Rich patents, would not have been motivated to provide a unit dose reagent chamber containing a detergent-containing buffered solution for use in a test

apparatus for detecting ATP in a test sample, by placing a detergent-containing buffered solution in the vessel of the Bernstein apparatus. The Bernstein apparatus features an open portal window and relies for its operation on the presence of a prefilter and capture membrane, and thus would not be suitable for use in ATP detection. Modification of the Bernstein apparatus to be suitable for ATP detection, by the substantial reconstruction of eliminating the prefilter and capture membrane, would result in leakage of unabsorbed fluid out of the window.

11. Based on my review of the Bernstein patent, it is my view that Bernstein sought to provide a test device suitable for performing a ligand receptor assay to detect antigens, haptens, antibodies, DNA or RNA fragment, wherein the user is not required to dispense any of the reagents. Further design criteria were that all reagents be self-contained within a device that could be stored at nonrefrigerated temperatures, and which could utilize lyophilized reagents. Bernstein, column 2, line 56, to column 3, line 2.

12. I further note that, at column 2, lines 46-55, Bernstein states that it is an object to transfer the reactants "to a reaction zone where the specific labeled reactant can be captured and visualized." I further note that, at column 1, paragragh 2, the Bernstein patent expresses the goal of eliminating any need for capital equipment such as "scintillation counters, flourometers and colorimeters in the case of radioimmunoassay, fluorescent immunoassay, and enzyme immunoassay respectively".

13. It is my opinion that the Bernstein apparatus is constructed so as to accomplish the goal of performing a rapid solid phase immunodiffusion assay. At column 3, lines 49-52,

Bernstein states that "[t]he configuration of the lower portion allows the collection device to come into physical contact with the prefilter, capture membrane or capture filter."

14. At column 2, lines 26-29, Bernstein states that "[i]n the case where membranes or filters are used to capture the immunoreactants, it is necessary to bring the fluid containing the immunoreactants in contact with the filter or membrane."

15. At column 2, lines 46-55, Bernstein further articulates the importance of having a larger pore size filter or membrane between the swab and capture membrane to retain any unwanted cells or debris that may interfere with the assay.

16. The Bernstein apparatus is also configured so that the assay results can be observed visually through a window, which is a discrete observation portal on the front side of the lower portion of the device. In order to visualize the signal without the aid of capital equipment, it was necessary to concentrate the signal in front of the window.

17. To concentrate the signal in front of the window Bernstein had to do four things: (a) capture the labeled members of the binding pair on capture membranes 18, 19; (b) eliminate interfering substances on a pre-filter membrane 25; (c) remove excess fluid on absorbent 17; and (d) deliver the reagents into direct proximity in front of the prefilter and reaction membranes. Bernstein, column 3, lines 34-51. I also note that, at column 5, lines 5-8, Bernstein states, "The shape of the lower portion 10 is configured to enhance contact of the collection device tip with the pre-filter or reaction membranes." Absent each of these design features, Bernstein would not be able to achieve sufficient signal enhancement for visualization through the front window 11.

18. It is my opinion that it would not have been obvious to one of ordinary skill in the art in 1995 to modify the Bernstein apparatus to be suitable for chemiluminescent detection of ATP with luciferin-luciferase. Adaptation of the Bernstein apparatus for chemiluminescent detection would have required modification of the device to be suitable for use with a luminometer. Those skilled in the art would not have found a suggestion or motivation to modify the Bernstein apparatus for use with a luminometer. To do so would have contradicted Bernstein's goal of providing a rapid immunodiagnostic assay that operated independently of capital equipment.

19. Another reason those skilled in the art would not have adopted the Bernstein apparatus for use with a luminometer is that, were one to do so, the Bernstein apparatus would have become inoperable for its intended purpose of visualization of signal by the naked eye. The shape of the lower portion of the Bernstein apparatus is configured to enhance contact of the collection device tip with the prefilter or reaction membranes. Bernstein, column 5, lines 5-7. Were the lower portion of the Bernstein apparatus to be modified to fit inside a luminometer, its shape would no-longer be configured to enhance contact of the collection tip with the prefilter or reaction membranes.

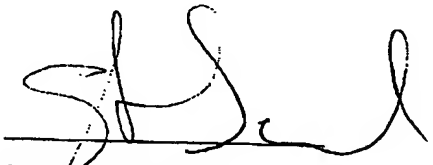
20. One skilled in the art would not have been motivated to modify the Bernstein apparatus to operate without prefilter or reaction membranes. Were the Bernstein apparatus to have been so adapted, there would be no concentration of signal in front of window 11, and the Bernstein apparatus would then be unsatisfactory for its intended purpose.

21. It is my opinion that one skilled in the art in 1995 would not have been motivated to place a detergent-containing buffered solution into the vessel of the Bernstein

device, because the Bernstein apparatus does not contain a closed bottom end. I note that, at column 5, lines 15-25, Bernstein describes an "adhesive tape 12 that holds the absorbent [17] in place and applies the necessary pressure to ensure diffusion of fluid through the various layers of the ligand receptor test area." The absorbent 17 absorbs excess fluid diffusing through the membranes. By removing adhesive tape 12 by lifting tab 28 of Bernstein, the bottom end of the Bernstein device is not a closed bottom end.

22. It is my opinion that one skilled in the art would not be motivated to undergo the substantial reconstruction of the Bernstein device that would be required to make it suitable for detecting ATP using a detergent-containing buffered solution. The bottom of the Bernstein device is not closed, so any solution would leak out the "window."

23. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.



Steven J. Saul, Ph.D

Date: 9/28/05

CURRICULUM VITAE

Name: STEVEN J. SAUL

Address: 11 Norfolk Road
Arlington, MA 02476

Education: Ph.D. Biological Science, University of Rhode Island, RI, 1983
A. B. Biology, Brown University, RI, 1977

Professional Experience:

2000-present	Director of Research, Charm Sciences Inc, Lawrence, MA
1990 -1999	Manager of Research, Charm Sciences, Inc., Malden, MA
1985 - 1990	Post-doctoral fellow, University of Massachusetts, Boston
1984 - 1985	Post-doctoral fellow, Children's Hospital, Boston
1979 - 1982	Instructor, University of Rhode Island
1977 - 1980	Graduate Res. Asst., University of Rhode Island

Publications:

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